REMARKS

If Applicants can help in any way to expedite this application, please contact the undersigned.

Respectfully submitted,
LYON & LYON LLP

Dated: March 13, 2002

By: _____
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MARKED-UP VERSION OF AMENDMENTS

IN THE SPECIFICATION:

1. On page 28, please substitute paragraph 0057 with the following paragraph:

[0057] It is possible to run the EM Merk Fractogel EMD 650(S) TMAE column in a displacement mode where super coiled plasmid displaces open circular plasmid off the resin, thereby enriching for super coiled plasmid. The column is equilibrated in 0.5 M NaC1, TE buffer, the load (neutralized lysis supernatant process 2) is diluted with 1.5 volumes WFI [WPI] then loaded onto the column. The column is loaded at 3.0 mg/ml resin. The last quarter of the flow through of the load to the TMAE column is recirculated over the column to allow SC plasmid to compete off open circular plasmid. The column is then washed to baseline with 0.5 M NaC1, TE after the recirculation has finished. The plasmid is then eluted with 1.9M $(NH_4)_2SO_4$.

2. On page 29, please substitute paragraph 0060 with the following paragraph:

[0060] The step-by-step methodology of Process I is outlined in Figure 2 [3].

3. On page 31, please substitute paragraph 0070 with the following paragraph:

[0070] The steps of Process II are outlined in Figure 3 [4]. Step (a) is fermentation of plasmid containing *E. coli,* cell harvesting, e.g. by centrifugation and washing and resuspending cells as in step 1 of Process I.

4. On Pge 39, please substitute paragraph 0089 with the following paragraph:

[0089] Previous purification of an α_1-antitrypsin plasmid prep had been done by the process 1 protocol (Fig. 2) [(Fig. 1)] in which the H.I.C. step had not yet been incorporated. Thus the purification process ended after the DEAE column step and the resulting plasmid pool was concentrated by standard ethanol precipitation. The final product of α_1-antitrypsin plasmid prepared by the above method still contained unacceptable high levels of chromosomal DNA (bacterial), RNA, denatured plasmid, and endotoxins.

5. On page 39, please substitute paragraph 0091 with the following paragraph:

[0091] Approximately 315 grams of DH-5α [D-5α] *E. coli* cells (wet weight) containing the α_1-antitrypsin plasmid was exposed to alkaline lysis for 5 minutes and the denatured chromosomal DNA/protein/sodium dodecylsulfate complexes were precipitated by addition of a salt solution containing 1.85M potassium acetate, 1.15M sodium chloride, 1.16M ammonium acetate at pH 5.5. After centrifugation, filtration, and RNAse treatment the resulting supernatant (8L) contained ~ 35 µg plasmid DNA/mL.